THE RELATIONSHIP OF APOPTOSIS AND IMPAIRED GENE EXPRESSION TO THE LOSS OF STRIATAL D_2-DOPAMINE RECEPTOR CONTAINING NEURONS DURING AGING

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Loss of dopaminergic motor control during aging is at least partially due to 30-50% reductions in concentrations of striatal D_2-dopamine receptors. Such decrements have been demonstrated in species ranging from rodents to humans and result from both loss of receptor containing neurons and reduced receptor synthesis in the surviving neurons. The latter is, in turn, due to age related reductions in D_2 receptor mRNA transcription.

A 19-27% loss of receptor containing neurons accounts for roughly half the D_2 receptor loss and is largely associated with cells susceptible to kainic acid toxicity in vivo. These neurons can be cultured from striata of neonatal rats and demonstrate similar selective vulnerability to kainate as well as the endogenous neurotransmitter, dopamine. In addition, the TUNEL assay for DNA fragmentation suggests that nearly half of the neuronal death in vivo may be apoptotic.

The precise causal relationship between impaired expression of the D_2 receptor gene and cell death remains to be elucidated. However, D_2 receptor loss during aging appears to be due to altered transcriptional regulation, the toxic effects of normal neurotransmission, and programmed cell death. Attempts to halt, prevent and/or reverse this loss by pharmacological, dietary and genetic manipulation are currently underway.

Source: https://www.industrydocuments.ucsf.edu/docs/gtdb0000